Amendment to the Claims:

This listing of claims will replace all prior versions, and listing, of claims in the application.

Listing of Claims:

1. (currently amended): The molecules selected ~~,~~ from those molecules derived from the combinatorial assembly of structural variations and common core, which, based on the use of validated molecular structural descriptors possessing the neighborhood property, do not share similar three dimensional shapes or likely activities ~~which possess desired properties~~, and which represent the chemical diversity that can be sampled with the structural variations and core but that do not over sample the diversity space, by the following computer-based method:

a) generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files, associated with the reaction identifying files, in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would

be combined in the listed combinatorial syntheses, which has not been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b) identifying in the virtual library all possible combinatorial product molecules which could result from the specified structural variations and selected core molecule;

c) selecting from all possible combinatorial product molecules a product molecule for inclusion in a ~~sub~~ set;

d) using a validated molecular descriptor appropriate to whole molecules with which the Virtual Library was generated, removing from the set of all remaining molecules those molecules falling within a chosen neighborhood distance of the selected molecule;

e) using a validated molecular descriptor appropriate to the structural variations with which the Virtual Library was generated, removing from the set of all remaining product molecules those molecules formed from structural variations falling within

a chosen neighborhood distance of the structural variations of the selected molecule;

f) selecting from the set of all product molecules remaining after step **e** a product molecule for inclusion in the ~~sub~~ set;

g) repeating steps **d** through **f** until no additional product molecules remain to be selected in step **f**; and

h) outputting a list of the selected ~~sub~~ set and/or the structural variations and core from which the ~~sub~~ set can be formed ~~.~~

wherein, based upon the use of validated molecular structural descriptors possessing the neighborhood property, the selected molecules do not have similar three dimensional shapes or activities and represent without oversampling the chemical diversity which can be sampled with the structural variations and core.

2. (currently amended): The molecules selected ~~,~~ from those molecules derived from the combinatorial assembly of structural variations and cores, which, based on the use of validated molecular structural descriptors possessing the neighborhood property, do not share similar three dimensional shapes or likely activities ~~which possess desired properties~~, and which represent the chemical diversity that can be sampled with the structural variations and cores but that do not over sample the diversity space, by the following computer-based method:

a) generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files, associated with the reaction identifying files, in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has not been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b) selecting from all possible cores a core upon which to base the ~~sub~~ set;

c) using a validated molecular descriptor appropriate to cores, selecting from the set of all possible cores those core molecules falling within a chosen neighborhood distance of the selected core molecule;

d) identifying all possible combinatorial product molecules which could result from

the specified structural variations and selected core molecule;

e) selecting from all possible combinatorial product molecules a product molecule for inclusion in the ~~sub~~ set;

f) using a validated molecular descriptor appropriate to whole molecules with which the Virtual Library was generated, removing from the set of all remaining molecules those molecules falling within a chosen neighborhood distance of the selected molecule;

g) using a validated molecular descriptor appropriate to the structural variations with which the Virtual Library was generated, removing from the set of all remaining product molecules those molecules formed from structural variations falling within a chosen neighborhood distance of the structural variations of the selected molecule;

h) selecting from the set of all product molecules remaining after step **g** a product molecule for inclusion in the ~~sub~~ set;

i) repeating steps **f** through **h** until no additional product molecules remain to be selected in step **h**; and

j) outputting a list of the selected ~~sub~~ set and/or the structural variations and cores from which the ~~sub~~ set can be formed ~~.~~

wherein, based upon the use of validated molecular structural descriptors possessing the neighborhood property, the selected molecules do not have similar three dimensional shapes or activities and represent without oversampling the chemical diversity which

can be sampled with the structural variations and cores.

3. (cancelled)

4. (cancelled)

5.(currently amended): The molecules having similar three dimensional shapes to the three dimensional shape of a molecule of interest and ~~,~~having a high probability , based on the use of validated molecular structural descriptors possessing the neighborhood property , of sharing an activity possessed ~~by a~~ by the molecule of interest , selected from those molecules derived from the combinatorial assembly of structural variations and a common core molecule, by the following computer-based method:

a) generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files, associated with the reaction identifying files, in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has not

been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b) identifying in the virtual library all possible combinatorial product molecules which could result from the specified structural variations and selected core molecule;

c) characterizing the molecule of interest with both a validated molecular structural descriptor appropriate to whole molecules with which the virtual library was generated and with a validated molecular structural descriptor appropriate to structural variations with which the virtual library was generated;

d) using the same validated molecular descriptor appropriate to whole molecules, selecting the set of all possible molecules whose descriptor values fall within a chosen neighborhood distance of the selected molecule, and using the same validated molecular descriptor appropriate to structural variations, selecting the set of all possible molecules whose descriptor values fall within a chosen neighborhood distance of the selected molecule; and

e) outputting a list of the selected ~~sub~~ set and/or the structural variations and core from which the ~~sub~~ set can be formed;

wherein , as determined by validated molecular structural descriptors possessing a neighborhood property, the three dimensional shape of the molecules in the selected ~~sub~~ set will be substantially similar to the three dimensional shape of the molecule of interest ~~as determined by the validated molecular structural descriptors~~ and will have a likelihood of possessing substantially similar activity to the molecule of interest.

6.(currently amended): The molecules having similar three dimensional shapes to the three dimensional shape of a molecule of interest and ~~,~~having a high probability , based on the use of validated molecular structural descriptors possessing the neighborhood property , of sharing an activity possessed ~~by a~~ by the molecule of interest , selected from those molecules derived from the combinatorial assembly of structural variations and a common core molecule, by the following computer-based method:

a) generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files, associated with the reaction identifying files, in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each

structural variation including:

(a). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has not been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b) identifying in the virtual library all possible combinatorial product molecules which could result from the specified structural variations and selected core molecule;

c) characterizing the molecule of interest with a combination validated molecular descriptor, characterizing both whole molecule and structural variation features, with which the Virtual Library was generated;

d) using the same validated molecular descriptor, selecting the set of all possible molecules whose descriptor values fall within a chosen neighborhood distance of the selected molecule; and

e) outputting a list of the selected ~~sub~~ set and/or the structural variations and core from which the ~~sub~~ set of molecules can be formed

wherein , as determined by validated molecular structural descriptors possessing a neighborhood property, the three dimensional shape of the molecules in the selected ~~sub~~ set will be substantially similar to the three dimensional shape of the molecule of interest ~~as determined by the validated molecular structural descriptors~~ and will have a likelihood of possessing substantially similar activity to the molecule of interest.

7.(currently amended): The molecules having similar three dimensional shapes to the three dimensional shape of a molecule of interest that is not known to be derived from a combinatorial reaction and ~~,~~having a high probability , based on the use of validated molecular structural descriptors possessing the neighborhood property , of sharing an activity possessed ~~by a~~ by the molecule of interest ~~that is not known to be derived from a combinatorial reaction~~, selected from those product molecules derived from the combinatorial assembly of structural variations and a common core molecule, by the following computer-based method:

a) generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files, associated with the reaction identifying files, in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has not been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b) fragmenting the molecule of interest as described in a fragmentation table;

c) selecting a fragmentation pattern;

d) aligning the fragments according to topomeric alignment rules;

e) generating CoMFA fields for each aligned fragment;

f) identifying which reaction types within the virtual library correspond to the reaction type resulting from the fragmentation;

g) identifying whether the fragmentation pattern generated a core, and, if so, implementing the following steps:

(1) characterizing the core with CoMFA fields; and

(2) identifying, by comparing the field values, whether the core resembles any cores used in the creation of the virtual library;

h) selecting structural variations which were used in generating the virtual library with cores which matched the core resulting from the fragmentation;

i) comparing the CoMFA fields of the topomerically aligned fragments with the fields of the identified structural variations by taking the root sum of squares field differences;

j) selecting those structural variations for which the root sum of squares field difference falls within a chosen neighborhood value;

k) ouputting a list of the selected ~~sub~~ set and/or the structural variations and cores from which the ~~sub~~ set can be formed;

l) repeating steps **c** through **k** for all possible fragments, and

wherein , as determined by validated molecular structural descriptors possessing a neighborhood property, the three dimensional shape of the molecules in the selected ~~sub~~ set will be substantially similar to the three dimensional shape of the molecule of interest ~~as determined by the validated molecular structural descriptors~~ and will have a likelihood of possessing substantially similar activity to the molecule of interest.

8. (new): The set of molecules selected from those molecules derived from the combinatorial assembly of structural variations and common core, which, based on the use of validated molecular structural descriptors possessing the neighborhood property, do not share similar three dimensional shapes or likely activities and which represent the chemical diversity

that can be sampled with the structural variations and core but that do not over sample the diversity space, by the following computer-based method:

a) generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files, associated with the reaction identifying files, in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has not been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b) identifying in the virtual library all possible combinatorial product molecules which could result from the specified structural variations and selected core molecule;

c) selecting from all possible combinatorial product molecules a product molecule for inclusion in a set;

d) using a validated molecular descriptor appropriate to whole molecules with which the Virtual Library was generated, removing from the set of all remaining molecules those molecules falling within a chosen neighborhood distance of the selected molecule;

e) using a validated molecular descriptor appropriate to the structural variations with which the Virtual Library was generated, removing from the set of all remaining product molecules those molecules formed from structural variations falling within a chosen neighborhood distance of the structural variations of the selected molecule;

f) selecting from the set of all product molecules remaining after step **e** a product molecule for inclusion in the set;

g) repeating steps **d** through **f** until no additional product molecules remain to be selected in step **f**; and

h) outputting a list of the selected set and/or the structural variations and core from which the set can be formed

wherein, based upon the use of validated molecular structural descriptors possessing the neighborhood property, the selected molecules do not have similar three dimensional shapes or activities and represent without oversampling the chemical diversity which can be sampled with the structural variations and core.

9. (new): The set of molecules selected from those molecules derived from the combinatorial assembly of structural variations and cores, which, based on the use of validated molecular structural descriptors possessing the neighborhood property, do not share similar three dimensional shapes or likely activities and which represent the chemical diversity that can be sampled with the structural variations and cores but that do not over sample the diversity space, by the following computer-based method:

a) generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files, associated with the reaction identifying files, in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would

be combined in the listed combinatorial syntheses, which has not been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b) selecting from all possible cores a core upon which to base the set;

c) using a validated molecular descriptor appropriate to cores, selecting from the set of all possible cores those core molecules falling within a chosen neighborhood distance of the selected core molecule;

d) identifying all possible combinatorial product molecules which could result from the specified structural variations and selected core molecule;

e) selecting from all possible combinatorial product molecules a product molecule for inclusion in the set;

f) using a validated molecular descriptor appropriate to whole molecules with which the Virtual Library was generated, removing from the set of all remaining molecules those molecules falling within a chosen neighborhood distance of the selected molecule;

g) using a validated molecular descriptor appropriate to the structural variations with

which the Virtual Library was generated, removing from the set of all remaining product molecules those molecules formed from structural variations falling within a chosen neighborhood distance of the structural variations of the selected molecule;

h) selecting from the set of all product molecules remaining after step **g** a product molecule for inclusion in the-set;

i) repeating steps **f** through **h** until no additional product molecules remain to be selected in step **h**; and

j) outputing a list of the selected set and/or the structural variations and cores from which the set can be formed

wherein, based upon the use of validated molecular structural descriptors possessing the neighborhood property, the selected molecules do not have similar three dimensional shapes or activities and represent without oversampling the chemical diversity which can be sampled with the structural variations and cores.

10.(new): The set of molecules having similar three dimensional shapes to the three dimensional shape of a molecule of interest and having a high probability based on the use of validated molecular structural descriptors possessing the neighborhood property of sharing an activity possessed by the molecule of interest , selected from those molecules derived from the combinatorial assembly of structural variations and a common core molecule, by the following computer-based method:

a) generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files, associated with the reaction identifying files, in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has not been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b) identifying in the virtual library all possible combinatorial product molecules which could result from the specified structural variations and selected core molecule;

c) characterizing the molecule of interest with both a validated molecular structural descriptor appropriate to whole molecules with which the virtual library was generated and with a validated molecular structural descriptor appropriate to structural variations with which the virtual library was generated;

d) using the same validated molecular descriptor appropriate to whole molecules, selecting the set of all possible molecules whose descriptor values fall within a chosen neighborhood distance of the selected molecule, and using the same validated molecular descriptor appropriate to structural variations, selecting the set of all possible molecules whose descriptor values fall within a chosen neighborhood distance of the selected molecule; and

e) outputting a list of the selected set and/or the structural variations and core from which the set can be formed;

wherein, as determined by validated molecular structural descriptors possessing a neighborhood property, the three dimensional shape of the molecules in the selected set will be substantially similar to the three dimensional shape of the molecule of interest and will have a likelihood of possessing substantially similar activity to the molecule of interest.

11.(new): The set of molecules having similar three dimensional shapes to the three dimensional shape of a molecule of interest and having a high probability based on the use of validated molecular structural descriptors possessing the neighborhood property, of sharing an activity possessed by the molecule of interest , selected from those molecules derived from the

combinatorial assembly of structural variations and a common core molecule, by the following computer-based method:

a) generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files, associated with the reaction identifying files, in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has not been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b) identifying in the virtual library all possible combinatorial product molecules which could result from the specified structural variations and selected core molecule;

c) characterizing the molecule of interest with a combination validated molecular descriptor, characterizing both whole molecule and structural variation features, with which the Virtual Library was generated;

d) using the same validated molecular descriptor, selecting the set of all possible molecules whose descriptor values fall within a chosen neighborhood distance of the selected molecule; and

e) outputting a list of the selected set and/or the structural variations and core from which the set of molecules can be formed

wherein, as determined by validated molecular structural descriptors possessing a neighborhood property, the three dimensional shape of the molecules in the selected set will be substantially similar to the three dimensional shape of the molecule of interest and will have a likelihood of possessing substantially similar activity to the molecule of interest.

12.(new): The set of molecules having similar three dimensional shapes to the three dimensional shape of a molecule of interest that is not known to be derived from a combinatorial reaction and having a high probability, based on the use of validated molecular structural descriptors possessing the neighborhood property, of sharing an activity possessed by the molecule of interest, selected from those product molecules derived from the combinatorial assembly of

structural variations and a common core molecule, by the following computer-based method:

a) generating a virtual library by:

(1). creating one or more files identifying one or more combinatorial reactions for one or more core structures;

(2). creating separate structural variation files, associated with the reaction identifying files, in which are listed together the structural variations representative of those reactants which will react at each variation site of each combinatorial reaction;

(3). associating with each structural variation, data, characterizing each structural variation including:

(a). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has not been derived from the application of validated molecular structural descriptors; and

(b). characterizing data, taking into account when necessary the structures of the cores with which the structural variations would be combined in the listed combinatorial syntheses, which has been derived from applying validated molecular structural descriptors to the structural variations;

b) fragmenting the molecule of interest as described in a fragmentation table;

c) selecting a fragmentation pattern;

d) aligning the fragments according to topomeric alignment rules;

e) generating CoMFA fields for each aligned fragment;

f) identifying which reaction types within the virtual library correspond to the reaction type resulting from the fragmentation;

g) identifying whether the fragmentation pattern generated a core, and, if so, implementing the following steps:

(1) characterizing the core with CoMFA fields; and

(2) identifying, by comparing the field values, whether the core resembles any cores used in the creation of the virtual library;

h) selecting structural variations which were used in generating the virtual library with cores which matched the core resulting from the fragmentation;

i) comparing the CoMFA fields of the topomerically aligned fragments with the fields of the identified structural variations by taking the root sum of squares field differences;

j) selecting those structural variations for which the root sum of squares field difference falls within a chosen neighborhood value;

k) ouputting a list of the selected set and/or the structural variations and cores from which the set can be formed;

l) repeating steps **c** through **k** for all possible fragments, and

wherein , as determined by validated molecular structural descriptors possessing a

neighborhood property, the three dimensional shape of the molecules in the selected set will be substantially similar to the three dimensional shape of the molecule of interest and will have a likelihood of possessing substantially similar activity to the molecule of interest.